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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/770,257	PESTANO, LINDA	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response to the Notice of Non-Responsive Amendment received on 10/15/08 has been entered. Claims 1-14 have been canceled. Claims 15-23 are currently pending and under examination at this time. Note that claim 23 was added with the amendment filed on 8/22/07. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Drawings

The submission of replacement sheets for Figures: 3A, 3B, 3C, 4A, 4B, 5, 6A, and 9B, on 8/22/07 is acknowledged. The replacements drawings are found to be in compliance with 37 CFR 1.121(d) and have been accepted by the examiner.

Claim Rejections - 35 USC § 112

The rejection of claims 1-2, 4-5, and 15-16 under 35 U.S.C. 112, first paragraph, for scope of enablement is withdrawn in view of the amendments to claim 15 and the cancellation of claims 1-2, and 4-5.

The rejection of claims 4-5, and 15-22 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn over canceled claims 4-5 and further over claims 15-22 in view of the amendments to these claims. It is also noted that applicant has stated for the record that claims 15-23 do not read on "in vivo" methods. "The method of the invention now comprises the contact of the monocytic dendritic cell precursors and the NK cells with GM-CSF and IL-15 followed by contact with the dendritic cell maturation agent. All of the steps take place outside of the body" (Applicant's response of 10/15/08, page 11 of 13, comments made to differentiate the claims as amended over Banchereau et al.).

Claim Rejections - 35 USC § 102

The rejection of claims 1-6 under 35 U.S.C. 102(b) as being anticipated by Mohamadzadeh et al. (2001) J.Exp. Med. 194:1013-1019, is withdrawn in view of the cancellation of these claims.

The rejection of claims 1-6, and 15-22 under 35 U.S.C. 102(b) as being anticipated by WO 01/85920 A2 (11/15/01), hereafter referred to as Banchereau et al., is withdrawn over canceled claims 1-6, and further over amended claims 15-22. It is noted that the claims have been amended such that they no longer read on "in vivo" contact between the NK cell and the dendritic cell. As indicated above, this has been stipulated by the applicant in their response to this rejection. "The method of the invention now comprises the contact of the monocytic dendritic cell precursors and the NK cells with GM-CSF and IL-15 followed by contact with the

dendritic cell maturation agent. All of the steps take place outside of the body" (Applicant's response of 10/15/08, page 11 of 13, comments made to differentiate the claims as amended over Banchereau et al.).

The rejection of claims 1, 6, 15, and 18-21 under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,849,452 (2/1/05), hereafter referred to as Zitvogel et al., is withdrawn over canceled claims 1 and 6 and further withdrawn over amended claims 15 and 18-21 in view of the amendments to the claims which now recite that the mature dendritic cells have been produced from monocytic dendritic cell precursor cells contacted with IL-15 and GM-CSF.

Applicant's claim amendments have necessitated the following new grounds of rejection under 35 U.S.C. 103.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-23 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,849,452 (2/1/05), hereafter referred to as Zitvogel et al., in view of WO 01/85920 A2 (11/15/01), hereafter referred to as Banchereau et al.

Zitvogel et al. teaches methods for inducing the activation of NK cells comprising contacting resting NK cells with mature dendritic cells *in vitro* or *ex vivo* (Zitvogel et al, columns 2-3, and columns 29-30, claims 1-11). Zitvogel et al. further teaches that the dendritic cells can be sensitized to one or more antigens (Zitvogel et al., column 12). Zitvogel et al. teaches that contact between the NK cell and dendritic cell can lead to the proliferation of the NK cell (Zitvogel et al., column 4 and column 16). Zitvogel et al. also teaches that the dendritic cells express IL-12, TNF-alpha, IL-15, and IFN α/β and that the NK cells can be part of a population of leukocytes prepared by leukopheresis, or a highly enriched population of resting NK cells comprising more than 70% resting NK cells (columns 13 and 20).

Zitvogel et al. differs from the instant invention by not teaching that the mature dendritic cells have been produced by contacting dendritic cell precursors with GM-CSF and IL-15. However, Zitvogel et al. does teach that the mature dendritic cells can be produced by culturing bone marrow, which comprises dendritic precursor cells, with GM-CSF and IL-4, followed by maturation induction with LPS (Zitvogel et al., columns 7, and 20). Banchereau et al.

supplements Zitvogel et al. by teaching that mature immunostimulatory dendritic cells can be produced by culturing dendritic cell precursors in the presence of GM-CSF and IL-15, and maturing the dendritic cells by treatment with LPS or CD40L (Banchereau et al., pages 8, 10, 12-13 and 19). Banchereau et al. further teaches that the mature dendritic cells produced from the culture of dendritic precursors in GM-CSF and IL-15 exhibited expression of CD1a, and high levels of CD80 and CD86 (Banchereau et al., page 13 and Figure 2a).Banchereau et al. also teaches exposing the dendritic cells to an antigen in the form of protein, peptides, or cells expressing the antigen (Banchereau et al., pages 11-13, and 25). Banchereau et al. further teaches that dendritic cells prepared with IL-15 and GM-CSF are similar in function to dendritic cells prepared with IL-4 and GM-CSF (Banchereau et al., page 22).

While Banchereau et al. did not do a direct comparison of the expression levels of CD1, CD80 and CD86 on dendritic cells produced from cultures in GM-CSF and IL-4, versus GM-CSF and IL-15, it is noted that the IL-15 dendritic cells of Banchereau et al. were produced using the same culture conditions, i.e. culture in IL-15 and GM-CSF, and appear to express the same markers as the cells recited in the instant methods. "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). Further, the applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to

establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Therefore, in view of the similarities in function between mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-15 and GM-CSF and those produced from cultures of dendritic precursor cells exposed to IL-4 and GM-CSF as taught by Banchereau et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-15 and GM-CSF taught by Banchereau for the mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-4 and GM-CSF in the methods of activating NK cells taught by Zitvogel et al. with a reasonable expectation of success that such a substitution would be capable of inducing the activation of NK cells in tissue culture.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the new technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633